

AMENDMENTS TO THE CLAIMS

This listing of the claims will replace all prior versions, and listings, of claims in this application.

Listing of Claims

1-24. **Canceled.**

25. **(Currently Amended)** A method of screening for compounds which reduce antibiotic resistance in a highly antibiotic resistant microbe comprising an AcrAB or AcrAB-like efflux pump, wherein the microbe comprises at least two of the following traits: i) at least one chromosomal mutation in a gene encoding an antibiotic target that renders the microbe resistant to one or more antibiotics; ii) a second mutation, ~~to~~ to the same gene or a different gene than in (i), ~~that~~ that further increases antibiotic resistance, and iii) increased expression of at least one efflux pump, comprising: contacting the microbe with a test compound and measuring the effect of the test compound on the activity of the AcrAB or AcrAB-like efflux pump, wherein compounds which inhibit the activity of the AcrAB or AcrAB-like efflux pump are identified as compounds which reduce antibiotic resistance in the microbe.

26. **(Previously Presented)** The method of claim 25, wherein the microbe comprises all three of the traits.

27. **(Previously Presented)** The method of claim 25, wherein the microbe is highly resistant to fluoroquinolones.

28. **(Previously Presented)** The method of claim 25, wherein the at least one chromosomal mutation is present in a gene selected from the group consisting of: gyrase and topoisomerase.

29. **(Previously Presented)** The method of claim 25, wherein the microbe is a Gram negative bacterium.

30. **(Previously Presented)** The method of claim 25, wherein the microbe further comprises functional porin channels.

31. **(Previously Presented)** The method of claim 25, wherein the microbe is contacted with test compounds selected from a library of test compounds.

32. **(Previously Presented)** The method of claim 25, wherein the activity of the AcrAB or AcrAB-like efflux pump is determined by measuring efflux of an indicator compound which is a substrate of the efflux pump.

33. **(Previously Presented)** The method of claim 25, wherein the activity of the AcrAB or AcrAB-like efflux pump is determined by measuring growth of the microbe in an antibiotic.

34. **(Previously Presented)** The method of claim 25, wherein the efflux pump is AcrAB.

35. **(Currently Amended)** A method of screening for compounds which specifically inhibit the activity of an AcrAB or AcrAB-like efflux pump comprising:

i) contacting a microbe comprising an AcrAB or AcrAB-like efflux and a non-AcrAB or non-AcrAB-like efflux pump and at least two of the following traits: i) at least one chromosomal mutation in a gene encoding a antibiotic target that renders the microbe resistant to one or more antibiotics; ii) a second mutation, (to the same gene or a different gene than in (i),) that further increases antibiotic resistance, and iii) increased expression of at least one efflux pump, with a test compound and an indicator compound;

ii) testing the ability of the test compound to inhibit the activity of the AcrAB or AcrAB-like efflux pump;

iii) testing the ability of the test compound to inhibit the activity of the non-AcrAB or non-AcrAB efflux pump;

iv) and identifying compounds which inhibit the activity of the AcrAB or AcrAB-like efflux pump relative to the non-AcrAB or non-AcrAB-like efflux pump to thereby identify compounds which specifically inhibit the activity of the AcrAB or AcrAB-like efflux pump.

36. **(Previously Presented)** The method of claim 35, wherein the microbe is highly antibiotic resistant.

37. **(Previously Presented)** The method of claim 35, wherein the microbe is highly resistant to fluoroquinolones.

38. **(Previously Presented)** The method of claim 35, wherein the at least one mutation is present in a gene selected from the group consisting of: gyrase and topoisomerase.

39. **(Previously Presented)** The method of claim 35, wherein the microbe is a Gram negative bacterium.

40. **(Previously Presented)** The method of claim 35, wherein the microbe further comprises functional porin channels.

41. **(Previously Presented)** The method of claim 35, wherein the microbe is contacted with test compounds selected from a library of test compounds.

42. **(Previously Presented)** The method of claim 35, wherein the activity of the AcrAB or AcrAB-like efflux pump is determined by measuring efflux of an indicator compound which is a substrate of the efflux pump.

43. **(Previously Presented)** The method of claim 35, wherein growth of the microbe in an antibiotic is measured.

44. **(Previously Presented)** The method of claim 35, wherein the efflux pump is AcrAB.

45. **(Currently Amended)** A method of treating an infection in a subject caused by a microbe comprising an AcrAB or AcrAB-like efflux pump and at least two of the following traits: i) at least one chromosomal mutation in a gene encoding a antibiotic target that renders the microbe resistant to one or more antibiotics; ii) a second mutation, ~~to~~ to the same gene or a different gene than in (i), ~~that~~ that further increases antibiotic resistance, and iii) increased expression of at least one efflux pump, comprising: contacting the microbe with an antibiotic to which the microbe is resistant and an inhibitor of an acrAB or acrAB-like efflux pump such that the infection in the subject is treated.

46. **(Previously Presented)** The method of claim 45, wherein the subject is treated prophylactically.

47. **(Previously Presented)** The method of claim 45, wherein the subject is treated therapeutically.

48. **(Previously Presented)** The method of claim 45, wherein the microbe is highly resistant to fluoroquinolones.

49. **(Previously Presented)** The method of claim 45, wherein the at least one mutation is present in a gene selected from the group consisting of: gyrase and topoisomerase.

50. **(Previously Presented)** The method of claim 45, wherein the microbe is a Gram negative bacterium.

51. **(Previously Presented)** The method of claim 45, wherein the microbe further comprises functional porin channels.